CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-456/458

ADMINISTRATIVE DOCUMENTS

FINAL ANDA APPROVAL SUMMARY

Note: ANDA 75-456 was tentatively approved on 1/24/00. Firm filed a Minor Amendment on 6/20/00 in accordance with the TA letter dated 1/24/00 stating that there have been no changes in the conditions under which the product was tentatively approved. Based on this amendment, ANDA 75-456 remains approvable.

ANDA:75-456 DRUG PRODUCT: Enalaprilat Injection (Carpuject)

FIRM: Abbott Laboratories DOSAGE FORM: Injection STRENGTH:1.25 mg/mL

CGMP STATEMENT/EIR UPDATE STATUS:
EER is acceptable as of 1/11/2000.

BIO STUDY: Satisfactory per Bio review dated 1/11/99 (P.M. Sathe). Bio waiver granted on 1/11/99.

VALIDATION - (DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S): Acceptable MV for the drug product was completed by the Phila.Dist Lab on 12/22/99 and the methods were found acceptable. The drug substance is a compendial item. FDA MV is not required.

STABILITY - (ARE CONTAINERS USED IN STUDY IDENTICAL TO THOSE IN CONTAINER SECTION?):

Three months of accelerated (40°C) and RT (25°-30°C) stability data are provided for the Enalaprilat Injection, 1.25 mg/mL, lot# PD8-056 (Splits A, B, and C), stored in a horizontal position. Data are within specs.

Containers used in the study are the same as those listed in the Container/closure section of the application.

LABELING: Satisfactory per Labeling review dated 3/2/99 (J.Barlow). FPL was reviewed by J. Barlow on 1/4/00 and was found acceptable.

STERILIZATION VALIDATION (IF APPLICABLE): Satisfactory per Micro review dated 8\2\99(L.A.Ensor)

SIZE OF BIO BATCH - (FIRM'S SOURCE OF NDS O.K.?):

NDS source: : Adequate

Bio batch size:

SIZE OF STABILITY BATCHES - (IF DIFFERENT FROM BIO BATCH WERE THEY MANUFACTURED VIA THE SAME PROCESS?):

Same as the biobatches.

PROPOSED PRODUCTION BATCH - (MANUFACTURING PROCESS THE SAME AS BIO/STABILITY?):

Proposed production batch size: liters

Manufacturing process is the same as those of the biobatches.

HFD-623/J.Fan/ 7/14/00
HFD-623/A.Mueller 7-7-00
V:\firmsam\abbott\ltrs&rev\75456n5.sum.doc
F/T by:

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 75-458 Date of Submission: October 28, 1998 & November 23, 1998.

Applicant's Name: Abbott Laboratories

Established Name: Enalaprilat Injection, 1.25 mg/mL (Vials)

Labeling Deficiencies:

1. CONTAINER - 1 mL and 2 mL vials

   Revise your container labels to include "Injection" rather than the abbreviation,"Inj."

2. CARTON

   Satisfactory in final print as of October 28, 1998 submission.

3. INSERT

   a. DESCRIPTION

      Its' molecular formula is ..[replace "empirical" with "molecular"]

   b. DOSAGE AND ADMINISTRATION

      Please note that USAN names are common nouns and should be treated as such in the text of labeling(i.e. lower case). Therefore, please revise "Enalaprilat Injection" to read "enalaprilat injection" throughout the text.

   c. CONTRAINDICATIONS

      First sentence - Revise to read as follows:

      ...converting enzyme inhibitor and in patients with hereditary or idiopathic angioedema.

   d. WARNINGS

      Neutropenia/Agranulocytosis - Revise as follows:

Marketing experience has revealed cases of neutropenia, or ...[delete the word "several"]

e. PRECAUTIONS

i. General - Revise to include the following as a new sub-subsection and to be the first paragraph of this subsection.

Aortic Stenosis/Hypertrophic Cardiomyopathy: As with all vasodilators , enalapril should be given with caution to patients with obstruction in the outflow tract of the left ventricle.

ii. Drug Interactions - Revise to include the following as a new sub-subsection and to be the third paragraph of this subsection directly following the "Agents Causing Renin Release" sub-subsection.

Non-steroidal Anti-inflammatory Agents: In some patients with compromised renal function who are being treated with non-steroidal anti-inflammatory drugs, the co-administration of enalapril may result in a further deterioration of renal function. These effects are usually reversible.

f. ADVERSE REACTIONS

Respiratory - Revise to read as follows:

...pulmonary infiltrates, eosinophilic pneumonitis [add "eosinophilic pneumonitis"]

g. OVERDOSAGE

Fourth paragraph, last sentence - Revise to include the following cross-reference and to read as follows:

...by peritoneal dialysis. (See WARNINGS, Anaphylactoid reactions during membrane exposure.)

Please revise your labels and labeling, as instructed above, and submit in final print.

Please note that we reserve the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

John L. Crawford

Robert L. West, M.S., R.Ph.
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

FINAL ANDA APPROVAL SUMMARY

Note: ANDA 75-458 was tentatively approved on 1/24/00. Firm filed a Minor Amendment on 6/20/00 in accordance with the 1/24/00 TA letter stating that there have been no changes in the conditions under which the product was tentatively approved. Based on this amendment ANDA 75-458 remains approvable.

ANDA:75-458 DRUG PRODUCT: Enalaprilat Injection (Vials)

FIRM: Abbott Laboratories DOSAGE FORM: Injection STRENGTH:1.25 mg/mL

CGMP STATEMENT/EIR UPDATE STATUS:
EER is acceptable as of 1/11/2000.

BIO STUDY: Satisfactory per Bio review dated 1/11/99 (P.M. Sathe).
Bio waiver granted on 1/11/99.

VALIDATION - (DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S):
Drug substance is a compendial item. Therefore, FDA MV is not required. Drug product is non-compendial. Therefore, MV is needed. However, analytical methods for the assay, Benzyl Alcohol and degradation products for ANDAs 75-458 (This application) and 75-456 are identical since they are sister applications. The only difference between the two applications are their container/closure systems (vials vs carpuject). The MV request for ANDA 75-456 was completed by the Phila.Dist.Lab on 12/22/99 and was found acceptable. Therefore, MV for ANDA 75-458 analytical methods (This application) is not deemed necessary.

STABILITY - (ARE CONTAINERS USED IN STUDY IDENTICAL TO THOSE IN CONTAINER SECTION?):

Three months of accelerated (40°C) and RT (25°-30°C) stability data are provided for the Enalaprilat Injection, 1.25 mg/mL, lot# PD8-057 and #PD8-058 (Splits A, B, and C), stored in an inverted position. Data are within specs.

Containers used in the study are the same as those listed in the Container/closure section of the application.

LABELING: Satisfactory per Labeling review dated 7/8/99 (J.Barlow). FPL was reviewed by J.Barlow on 1/4/00 and was found acceptable.

STERILIZATION VALIDATION (IF APPLICABLE): Satisfactory per Micro Review dated 8\4\99(L.A.Ensor)

SIZE OF BIO BATCH - (FIRM'S SOURCE OF NDS O.K.?):

NDS source: : Adequate

Bio batch size: Lot PD8-057 and PD8-058

SIZE OF STABILITY BATCHES - (IF DIFFERENT FROM BIO BATCH WERE THEY MANUFACTURED VIA THE SAME PROCESS?):

Same as the biobatches.

PROPOSED PRODUCTION BATCH - (MANUFACTURING PROCESS THE SAME AS BIO/STABILITY?):

Proposed production batch size: liters
Manufacturing process is the same as those of the biobatches.